

# An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI)<sub>†</sub>

Update on the Use of Pneumococcal Vaccines:  
Addition of Asthma as a High-Risk Condition

PROTECTING CANADIANS FROM ILLNESS



Public Health  
Agency of Canada

Agence de la santé  
publique du Canada

Canada

**TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH LEADERSHIP, PARTNERSHIP,  
INNOVATION AND ACTION IN PUBLIC HEALTH.**

—Public Health Agency of Canada

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## PREAMBLE

The National Advisory Committee on Immunization (NACI) provides the Public Health Agency of Canada (hereafter referred to as the Agency) with ongoing and timely medical, scientific, and public health advice relating to immunization. The Agency acknowledges that the advice and recommendations set out in this statement are based upon the best current available scientific knowledge and is disseminating this document for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph(s). Recommendations for use and other information set out herein may differ from that set out in the product monograph(s) of the Canadian manufacturer(s) of the vaccine(s). Manufacturer(s) have sought approval of the vaccine(s) and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of the Agency's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

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## SUMMARY OF INFORMATION CONTAINED IN THIS NACI STATEMENT

The following table highlights key information for immunization providers. Please refer to the remainder of the Statement for details

<p><b>1. What</b></p>	<p><b>What is Pneumococcal Disease?</b>  <i>Streptococcus pneumoniae</i> is a Gram-positive bacterium that is known to cause invasive disease such as sepsis, meningitis and pneumonia. Symptoms depend on the site of infection. It is a major cause of morbidity and mortality in children, the elderly population, and individuals with immunosuppression and other chronic conditions. Additional information can be found on the <u>Public Health Agency of Canada website</u> (<a href="http://www.phac-aspc.gc.ca/im/vpd-mev/pneumococcal-eng.php">http://www.phac-aspc.gc.ca/im/vpd-mev/pneumococcal-eng.php</a>)</p> <p><b>What are pneumococcal vaccines?</b>  Two forms of pneumococcal vaccine are available; a conjugated vaccine (PNEU-C-10 and PNEU-C-13) and a polysaccharide vaccine (PNEU-P-23).</p>
<p><b>2. Who</b></p>	<p><b>Who should be immunized?</b>  Individuals requiring medical attention for asthma in the last 12 months regardless of whether they are on high dose steroids or have chronic obstructive pulmonary disease (COPD).</p> <p>This recommendation is in addition to the previously published recommendations in the <u>Canadian Immunization Guide</u> (<a href="http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php">http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php</a>)</p> <p>Recommendations for children are available on the <u>NACI website</u> (<a href="http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-12/index-eng.php">http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-12/index-eng.php</a>)</p> <p>Recommendations for the use of the 13-valent pneumococcal vaccine are available on the NACI website (<a href="http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-5/index-eng.php">http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-5/index-eng.php</a>)</p>
<p><b>3. How</b></p>	<p><b>Dose and Schedule</b>  As currently recommended for <u>other high-risk conditions</u>, without immunosuppression (<a href="http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php">http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php</a>)</p> <ul style="list-style-type: none"> <li>• Children 2 to 18 years of age with asthma should receive PNEU-C-13 as appropriate for their age group and an additional dose of PNEU-P-23 at least 8 weeks after the last dose of PNEU-C-13.</li> <li>• Adults with asthma should receive one dose of PNEU-P-23.</li> </ul> <p>At this time further booster doses of PNEU-C-13 or PNEU-P-23 are not recommended.</p>

4. Why	<p>Current evidence indicates that asthma is a risk factor for invasive pneumococcal disease, even in the absence of prolonged systemic corticosteroid use or COPD.</p> <p>Pneumococcal infection can cause severe disease.</p> <p>The most effective way to prevent these infections is through immunization.</p>
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## I. INTRODUCTION

This statement will supplement previous pneumococcal statements<sup>1-4</sup> and provide the evidence used to add asthma to the group of conditions that increase an individual's risk for invasive pneumococcal disease (IPD).

This update will:

- Provide a systematic review of the literature on the risk of IPD associated with asthma;
- Make recommendations about the use of pneumococcal vaccines in individuals with asthma

## II. METHODS

NACI reviewed<sup>5</sup> such considerations as the burden of disease and the target population, safety, immunogenicity, efficacy, effectiveness of the vaccines, vaccine schedules, and other aspects of the overall immunization strategy when available. Following critical appraisal of individual studies,<sup>6</sup> summary tables with ratings of the quality of the evidence were prepared using NACI's methodological hierarchy (Tables 7 and 8), and proposed recommendations for vaccine use were developed. The Working Group chair presented the evidence and proposed recommendations to NACI. Following thorough review of the evidence and consultation at NACI meetings (June 6 and October 10, 2013), the committee voted on specific recommendations. The description of relevant considerations, rationale for specific decisions, and knowledge gaps are described in the text of this update. The Agency maintains documentation of these processes throughout knowledge synthesis and recommendation development.

## III. EPIDEMIOLOGY OF PNEUMOCOCCAL DISEASES IN CANADA AND RISK OF IPD IN ASTHMATICS

### III.1 Disease Description

Invasive pneumococcal disease (IPD) is a serious illness caused by the bacterium *Streptococcus pneumoniae*. There are currently 92 serotypes recognized worldwide, 15 of which cause the majority of disease. *S. pneumoniae* can be spread from an infected person to another person by droplets from the nose or mouth, by sneezing or coughing. Infections caused by *S. pneumoniae* are a major cause of morbidity and mortality worldwide. It is estimated that approximately one million children die of pneumococcal disease each year; the majority of which are young children in developing countries. In developed countries the highest incidence of IPD is in young children under 2 years of age. A large burden of disease also exists among elderly persons.<sup>7</sup> (<http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-5/index-eng.php>)

Children and adults often are asymptomatically colonized with *S. pneumoniae* in their upper respiratory tract and nasopharynx. IPD is a severe form of infection that occurs when the bacterium invades normally sterile sites, such as the bloodstream and central nervous system. The symptoms or clinical manifestations depend on the site of infection. Invasive disease may

lead to several syndromes including bacteremia, meningitis, and/or bacteremic pneumonia (with or without empyema).

Certain medical conditions have been recognized to put individuals at increased risk of pneumococcal disease. The currently recognized conditions include: sickle cell disease and other haemoglobinopathies, chronic kidney disease including nephrotic syndrome, chronic liver disease, chronic cardiac or pulmonary disease, immunosuppression, anatomic or functional asplenia, chronic cerebrospinal fluid leaks, cochlear implants, chronic neurologic conditions that may impair clearance of oral secretions, diabetes mellitus and HIV infection. However, asthma was only considered a high-risk condition when accompanied by long-term systemic corticosteroid use or chronic obstructive pulmonary disease.

### III.2 Prevalence of Asthma

The proportion of Canadians aged 12 years and over who report having been diagnosed by a healthcare professional as having asthma is around 10%. For the years 2008 to 2012: 10.2 to 11.8% of the 12-19 year-olds, 9.1 to 9.7% of the 20 to 34 year-olds, 6.8 to 8% of the 35 to 44 year-olds and 6.3 to 8.1% of the 45 to 64 year-olds were considered asthmatics (Source: Statistics Canada).

### III.3 Incidence rates of Invasive Pneumococcal Disease (IPD)

Table 1 details the IPD incidence rates by age group and year in Canada from 2001 to 2011. Although specific provincial and territorial IPD rates stratified by age groups need to be looked at in more detail, because the epidemiology of IPD varies across the country, the average Canadian IPD incidence rates show that rates are highest in the 0-4 years age group, followed by the 60+ age group – these age groups (0-4 years and 65 years and over) are currently routinely vaccinated against IPD. Canadians aged 10 to 59 years have an absolute risk of IPD that is much lower (IPD rates < 10 per 100,000 individuals).

**Table 1. Incidence rate (per 100,000) of invasive pneumococcal disease by age group and year, Canada, 2001-2011**

Year	Age Groups									
	<1	1 to 4	5 to 9	10 to 14	15 to 19	20 to 24	25 to 29	30 to 39	40 to 59	60+
2001	37.37	25.17	3.62	1.06	1.47	1.57	1.83	2.52	4.13	10.75
2002	50.00	33.38	3.17	1.56	1.18	1.59	2.11	3.47	4.69	15.55
2003	54.51	35.55	4.36	1.17	0.99	1.38	3.00	4.74	6.49	18.33
2004	42.90	30.97	4.25	1.17	1.26	1.63	2.83	4.93	7.60	20.68
2005	25.94	21.38	5.26	1.79	1.29	2.60	3.21	4.97	8.10	20.40
2006	19.99	13.73	4.55	1.81	1.81	1.95	3.75	6.76	9.04	19.10
2007	30.26	15.68	3.44	1.95	2.10	3.39	4.53	7.12	10.23	20.45
2008	29.75	16.56	4.57	1.44	1.37	2.67	3.45	5.17	9.60	21.51
2009 <sup>†</sup>	27.74	18.57	5.78	1.62	1.78	2.33	3.41	5.44	8.89	22.25
2010 <sup>†</sup>	24.82	16.37	4.71	1.86	1.26	1.82	3.09	5.09	8.98	23.26
2011 <sup>†</sup>	20.65	15.34	5.20	2.42	1.64	1.37	2.97	5.33	9.10	21.57

<sup>†</sup> A total of 43 cases with age missing are excluded from this table.

There is currently no Canadian data on the risk of IPD in individuals with asthma, except for data from the Canadian Immunization Monitoring Program Active (IMPACT) program in children. This surveillance system has been collecting information on IPD with specific questions about asthma and wheezing since 2005. Data collected includes use of daily steroids as a proxy measure of disease severity as well as wheezing associated with an IPD illness. In children aged 5 years and over, the prevalence of asthma varies from 6.5 to 12% of IPD cases, while wheezing in the week prior to IPD occurred in 5 to 9% of children 0 to 16 years of age (Table 2).

**Table 2. Characteristics of IPD cases**

Age Group	N	Asthma/ Wheezing as underlying health condition N (%)	Wheezing in prior week N (%)	Treated for wheezing N (%)	Daily steroid use for wheezing N (%)	Type of steroid		
						Oral	Aerosol	Both
< 12 mo	275	0 (0)	12 (4.36)	7 (2.55)	6 (2.18)	0 (0)	5 (1.82)	1 (0.36)
1-4 y	594	43 (7.24)	54 (9.09)	37 (6.23)	22 (3.7)	3 (0.51)	16 (2.69)	3 (0.51)
5-9 y	235	29 (12.34)	15 (6.38)	11 (4.68)	9 (3.83)	1 (0.43)	7 (2.98)	1 (0.43)
10-16 y	120	8 (6.67)	6 (5)	5 (4.17)	1 (0.83)	0 (0)	1 (0.83)	0 (0)
Total	1224	80 (6.54)	87 (7.11)	60 (4.9)	38 (3.1)	4 (0.33)	29 (2.37)	5 (0.41)

Source: Julie Bettinger, IMPACT

Tables 3 and 4 show that in children with IPD who reported wheezing in the prior week, the majority of had another underlying medical condition in addition to asthma (64.4% of cases). This is particularly true in children aged less than 10 years of age.

**Table 3. Underlying health status for IPD cases with wheezing in the prior week**

Age Group	Underlying Health Status						Total	
	Healthy		Asthma Only		Other conditions			
	N	%	N	%	N	%	N	%
< 12 months	0	0.0	0	0.0	12	100.0	12	13.8
1-4 years	0	0.0	21	38.9	33	61.1	54	62.1
5-9 years	1	6.7	5	33.3	9	60.0	15	17.2
10-16 years	0	0.0	4	66.7	2	33.3	6	6.9
Total	1	1.1	30	34.5	56	64.4	87	100.0

**Table 4. Underlying Health status for IPD cases given medication for wheezing**

Age Group	Underlying Health Status						Total	
	Healthy		Asthma Only		Other conditions			
	N	%	N	%	N	%	N	%
< 12 months	0	0.0	0	0.0	7	100.0	7	11.7
1-4 years	0	0.0	17	45.9	20	54.1	37	61.7
5-9 years	0	0.0	3	27.3	8	72.7	11	18.3
10-16 years	0	0.0	4	80.0	1	20.0	5	8.3
Total	0	0.0	24	40.0	36	60.0	60	100.0

Source: Julie Bettinger, IMPACT

Based on IMPACT data, the number of IPD cases with asthma either admitted to hospital or treated as outpatients is quite low (6.5%), with the majority of cases in children 1-4 years of age. These children would already be immunized under current immunization recommendations.

The frequency of asthma among 5-9 year olds with IPD (12.3%) is similar to the population rates of asthma generally reported for this age group (10%-15%).<sup>8</sup> Of note, fewer than half of these cases (14/29) had wheezing at the onset of their pneumococcal infection. IPD cases with asthma often had a second health condition that might have increased the risk for infection, but which also place them in a risk group that should already be vaccinated (e.g. sickle cell, immunosuppressing conditions).

### III.4 Risk of IPD in Children with Asthma (Table 6)

**Table 5** summarizes the studies that are detailed further in the following section. Detailed information about each study can be found in **Table 6** at the end of the statement.

Author	Number of patients	Asthma: Point estimate (95% CI)
Pilishvili <sup>9</sup>	US children – cases of IPD: 782, controls: 2512	OR 1.5 (1.1-2.1)
Hsu <sup>10</sup>	US children – 578 cases of IPD; 3% were asthmatics not on systemic corticosteroids	65% of IPD cases that were asthmatics presented with pneumonia compared to 31% of IPD cases with no risk factor ( $p < 0.05$ )
Hjuler <sup>11</sup>	Danish children – 1,655 cases of IPD; 15, 373 controls	Adjusted RR 1.1 (0.7-1.6)
Flory <sup>12</sup>	US adults – 609 with bacteremic pneumococcal pneumonia	Incidence 21.1 (16.7-26.6) in asthmatics vs. 8.8 (7.9-9.8) per 100,000 population
Klemets <sup>13</sup>	Finnish adults – 1282 cases of IPD; 12785 controls	Low-risk asthma: matched OR 2.8 (2.1-3.6) High-risk asthma: matched OR 12.3 (5.4-28.0)
Watt <sup>14</sup>	Navajo adults – 118 cases of IPD; 353 controls	Matched univariable OR 1.3 (0.6-2.9)
Juhn <sup>15</sup>	US children and adults with severe pneumococcal disease – 174 cases with SPD (66 had IPD, others had pneumococcal pneumonia only); 348 controls	All age: OR 2.4 (0.9-6.6) Adults: OR 6.7 (1.6-27.3)
Talbot <sup>16</sup>	US citizens aged 2-49 years – 635 cases of IPD; 6350 controls	Any asthma: OR 2.4 (95% CI: 1.9-3.1) High-risk asthma: OR 2.6 (95% CI: 2.0-3.5) Low-risk asthma: OR 1.7 (1.0-3.0)

Pilishvili et al<sup>9</sup> conducted a population- and laboratory-based case-control study with a group of 3,294 American children aged 3-59 months. Cases were identified through routine Active Bacterial Core (ABC) surveillance of IPD in California, Colorado, Georgia, Minnesota, New York, Oregon, Tennessee and Connecticut. Three controls were matched to each case on the basis of age and mother's residential zip code at time of birth. Health care providers, "from whom children reportedly received routine medical care and immunizations,"<sup>9</sup> ascertained information on underlying illnesses, including asthma status, for all study participants. This study found that IPD case patients with non-PCV7 type IPDs were more likely than controls to have asthma (Odds ratio [OR] 1.5; 95% Confidence Interval [CI], 1.1-2.1).

Hsu et al<sup>10</sup> conducted a retrospective population-based study to determine the underlying conditions predisposing Massachusetts' children aged <18 years old to IPD in the PCV-7 vaccine era between October 1, 2001 and September 30, 2007. Cases of IPD were ascertained using microbiology laboratory reports. Cases classified as "high risk" or "probable high risk" for IPD included, among others, children with chronic pulmonary disease, which included asthmatics treated with high dose oral corticosteroids. Children with asthma not receiving corticosteroid therapy were evaluated separately. Probable high-risk children with asthma receiving oral corticosteroid therapy represented 3% of the 578 cases that had sufficient information about underlying diseases. The clinical presentation of IPD in children with high-risk/probable high-risk conditions was similar to children with no known risk factor except for an increased risk of pneumonia in children with asthma: 65% of children with asthma presented with pneumonia compared to only 31% of children with no known risk factors ( $P<0.05$ ). Moreover, after adjusting for age and study year, children classified as 'high risk' (i.e. conditions such as asplenia and HIV) had 2.17 times the odds (95% CI: 1.44-5.24) of being hospitalized for IPD compared to children classified as 'probable high risk' (i.e. asthma with oral steroids and congenital immune deficiencies).

Hjuler et al<sup>11</sup> conducted a nested case-control study within the Danish population aged 0-17 years aiming to quantify the risk of IPD in a wide range of chronic diseases, including asthma ( $n=17\ 028$  children in total, of which 60 cases with IPD and 282 controls without IPD had asthma). Cases of IPD between January 1977 and May 2005 were selected from the Danish Streptococcus Database. Ten age- and gender-matched population controls were randomly sampled per case from the Danish Civil Registration System. Ascertainment of chronic diseases (including asthma status) was obtained from the National Registry of Patients. Risk ratios were adjusted for hospital contacts for any reason within the last 3-30 days. This study found an IPD rate ratio (adjusted for the number of hospital contacts) of 1.1 (95% CI 0.7, 1.6) in asthmatic children compared to control children without asthma on record.

### III.5 Risk of IPD in Adults with Asthma (Table 6)

Flory et al<sup>12</sup> conducted a prospective population-based surveillance study to evaluate the association between bacteremic pneumococcal pneumonia (BPP), asthma and socioeconomic risk factors. Specifically, 43 of 46 acute care hospitals in the 5-county region surrounding Philadelphia between March 31 2002 and April 1 2004 participated in the study. Cases were eligible for inclusion if they were 18 years or older "with at least one blood culture within 48 hours of hospital admission positive for *S.pneumoniae*; a clinical diagnosis of pneumonia provided by the treating physician; residence in one of the five counties; and confirmation in a reference laboratory that the isolated strain was *S.pneumoniae*."<sup>12</sup> Each case underwent a 30-minute structured interview. The annual incidence of BPP was calculated using annual census data as a denominator and Poisson distribution confidence intervals. Of the 609 cases of BPP,

281 subjects completed the telephone interview and 25% of 281 subjects had been diagnosed with asthma. The reported incidence of BPP was 21.1 (95% CI: 16.7, 26.6) cases per 100,000 person years for individuals with a history of asthma compared to 8.8 per 100 000 person years (95% CI, 7.9-9.8) for individuals without a history of asthma.

Klemets et al<sup>13</sup> conducted a nationwide registry- and population- based case-control study in order to establish the risk of IPD among adults with asthma in Finland. Cases of IPD, (defined by the isolation of *S.pneumoniae* from blood or cerebrospinal fluid), were ascertained from national population-based laboratory surveillance from 1995 to 2002. Only first episodes of IPD among adults aged 18-49 were included in the study to reduce confounding due to smoking-related lung disease and COPD that are more likely to occur in individuals aged 50 and over. Ten controls without IPD were randomly selected from the National Population Information System and matched to each case based on age, sex and health district of residence. Patients and controls with asthma were defined in this study as "persons who had been granted a prescription drug benefit for asthma or COPD by the Finnish National Social Insurance Institution, or who had a record of hospitalization for these conditions during 12 months before the reference date in the National Hospital Discharge Register database."<sup>13</sup> More specifically, the Finnish National Social Insurance Institution uses the following criteria to determine a patient's eligibility for prescription drug benefit: a physician's certificate verifying the diagnosis as well as the severity of illness using lung function tests (such as spirometry) as well as the need for prescription medications for at least 6 months. Asthma status was defined as persons with  $\geq 1$  hospitalization due to asthma (National Hospital Discharge Register) or persons who were granted a prescription drug benefit for asthma (National Social Insurance Institution) in the 12 months prior to the reference date. High-risk asthmatics were people who were hospitalized at least once for asthma in the past 12 months. Low-risk asthmatics were those not hospitalized, but entitled to asthma prescription drug benefit during the 12 months before the reference date. Asthma status was ascertained by linking the case-control study database to four other national population-based healthcare registries. Overall, Klemets et al reported that patients with IPD were more likely than controls to have low-risk asthma (matched OR 2.8 [95% CI, 2.1-3.6]) and high-risk asthma (matched OR 12.3 [95% CI, 5.4-28.0]). The results from this study support asthma – both low and high risk – as an independent risk factor for IPD in adults aged 18-49 years.

Watt et al<sup>14</sup> conducted a matched case-control study of Navajo adults (>18 years old) in the US Navajo population to identify risk factors for IPD (n=471 adults, of which 8 cases with IPD and 19 controls without IPD had asthma). Study participants were identified through prospective, population-based active laboratory surveillance (date of *S.pneumoniae* culture between December 1999-February 2002) and asthma status was ascertained from medical record data. Controls were matched to cases based on age, gender, and neighborhood. Asthma status was ascertained through a structured interview. A matched univariate analysis was used to identify possible risk factors for IPD in this population. This study found that the odds of having IPD were 1.3 (95% CI 0.6, 2.9) times higher in asthmatics compared to non-asthmatics.

### III.6 Risk of IPD in Adults and Children with Asthma (Table 6)

The following two studies included both adults and children and are reported separately.

Juhn et al<sup>15</sup> conducted a population-based retrospective case-control study evaluating whether asthma status was associated with serious pneumococcal disease (SPD). They reviewed medical records of 3,941 residents of Rochester, Minnesota between 1964 and 1983 to

ascertain SPD, asthma status and identified potential cases of IPD. Cases of SPD were then confirmed by medical records review and defined as individuals with an isolation of *S.pneumoniae* from a normally sterile site or pneumococcal pneumonia requiring all of the following three criteria: 1) a physician's diagnosis of pneumonia, 2) identification of pneumococcus from sputum Gram stain or in culture, and 3) pneumonia documented by means of chest radiography. Two controls were matched to every case by gender and date of birth. Exposure ascertainment (i.e. asthma status) was obtained by merging SPD case and control data with data collected from a previous study. Briefly, using the medical diagnostic list within the Rochester Epidemiology Project, potential cases of asthma were identified and all medical records were reviewed to confirm asthma. Diagnostic categories have been linked across the many updates of the diagnostic indices, including revisions of the ICD. From the 18,000 potential asthma cases, 2499 patients met the criteria for asthma. Using a conditional logistic regression model for matched analysis, the authors showed that SPD was associated with a prior history of asthma (OR 2.4; 95% CI, 0.9-6.6) among all age groups including adults (OR 6.7; 95% CI, 1.6-27.3), controlling for high-risk conditions for IPD and smoking exposure. Results from this study suggest that asthma increases risk for serious pneumococcal disease.

Talbot et al<sup>16</sup> examined the association between asthma and IPD by conducting a nested matched case-control study of 6,985 residents of Tennessee aged 2-49 years of age during the study period 1995 to 2002. Data from the ABC Surveillance were used to identify eligible study participants with IPD. Once identified, ABC data was linked to administrative data from the Tennessee Medicare (TennCare) program. Ten age-matched controls without IPD were randomly matched to each case from the same population. Asthma status was ascertained by screening inpatient and outpatient claims for all participants for a diagnosis of asthma based on the ICD-9-CM code (section 493). Participants with asthma were classified as either high risk ("a history of one or more hospitalizations or visits to an emergency department for asthma or who were given a prescription for a course of corticosteroids as rescue therapy or a long-term course of oral corticosteroids (120 days or more) or prescriptions for three or more  $\beta$ -agonist medications during the year before the index date")<sup>16</sup> or low-risk (all other participants with asthma). After adjusting results for sex, race, and high-risk co-existing conditions, the authors showed that any diagnosis of asthma was associated with an increased risk of IPD (OR 2.4; 95% CI: 1.9-3.1). This association persisted when results were stratified by asthma severity: patients with a classification of high-risk asthma had 2.6 times the odds of IPD compared to controls (95% CI: 2.0-3.5) while patients with a classification of low risk asthma had 1.7 times the odds of IPD (95% CI: 0.99-3.0) as compared to controls. It should be noted that while misclassification of asthma status in this study was possible, such misclassification would have been non-differential for cases and controls, biasing the study results towards the null hypothesis and potentially underestimating risk of IPD in asthmatics.

## IV. VACCINE

### IV.1 Preparation(s) authorized for use in Canada

#### Conjugate pneumococcal vaccines

- **Pneumovax®13:** pneumococcal 13-valent conjugate vaccine, CRM<sub>197</sub> protein conjugate adsorbed, Pfizer Canada Inc. (licensee) (Pneu-C-13)

The diphtheria carrier protein used in conjugate pneumococcal vaccines does not confer protection against diphtheria.

- **SYNFLORIX®:** pneumococcal 10-valent conjugate vaccine, non-typeable *Haemophilus influenzae* protein D, diphtheria or tetanus toxoid conjugates adsorbed, GlaxoSmithKline Inc. (Pneu-C-10).

The tetanus, diphtheria and non-typeable *Haemophilus influenzae* carrier proteins used in conjugate pneumococcal vaccines do not confer protection against diphtheria, tetanus or *Haemophilus influenzae* type b disease.

#### Pneumococcal 23-valent polysaccharide vaccines

1. **PNEUMOVAX®23:** pneumococcal 23-valent polysaccharide vaccine, Merck Canada Inc. (Pneu-P-23)
2. **PNEUMO 23®:** pneumococcal 23-valent polysaccharide vaccine, Sanofi Pasteur SA (manufacturer), sanofi pasteur Ltd. (distributor) (Pneu-P-23)

For complete prescribing information, consult the product leaflet or information contained within Health Canada's authorized product monograph available through the [Drug Product Database](#). Refer to the Canadian Immunization Guide for more information on pneumococcal serotypes covered in each vaccine (<http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php#approve>)

#### IV.2 Efficacy – direct and indirect

There are currently no efficacy data on the use of pneumococcal vaccines specifically for individuals with asthma.

#### IV.3 Effectiveness

There are currently no data on the effectiveness of pneumococcal vaccines specifically for individuals with asthma. Please refer to previous NACI statements on pneumococcal vaccines for data in the general population (**PCV in adults:** <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-5/index-eng.php>, **Children :** <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs12/index-eng.php>, and **CIG:** <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php>)

#### IV.4 Immunogenicity

There are currently no good data on the immunogenicity of pneumococcal vaccines specifically for individuals with asthma. A low quality study published by Jung et al<sup>17</sup> compared serotype specific antibody responses with pneumococcal polysaccharide antigens of individuals with and without asthma. Sixteen subjects with asthma (median age 20 years) and 14 subjects without asthma (median age 28 years) were included in the study. Asthma status was based on a comprehensive review of medical record. Serotype-specific antibody to 23 pneumococcal polysaccharide antigens was measured by enzyme-linked immunosorbent assay and seropositivity was defined as  $\geq 1.3 \mu\text{g/mL}$ . At the time of study, the proportion of participants who were colonized in their nasopharynx with *S.pneumoniae* was similar in both groups. The median numbers of positive serotype-specific antibodies for individuals with asthma was 8.5, compared to 15.5 in non-asthmatics. Seven (44%) of 16 asthmatics compared to 12 (86%) of 14

non-asthmatics had 12 or more positive serotype-specific antibodies. The authors did not show any data on previous IPD. The only data available on vaccination status was to say that 4 (25%) asthmatics and 3 (21.4%) non-asthmatics had previously been vaccinated with PNEU-C-7 and 4 (25%) and 1 (7.1%) of asthmatics and non-asthmatics, respectively, had received one dose of PNEU-P-23, but without specifying when the doses were administered. In a more recent paper, using the same study population and serum samples, the same group of authors reported that both groups (with and without asthma) had a similar antibody response to cell surface pneumococcal protein antigen and intracytoplasmic pneumococcal antigen.<sup>18</sup>

## V. SUMMARY

The studies reviewed suggest that adults with asthma (whether high-risk or low-risk) are more likely to present with IPD compared to adults without asthma; this association seems less obvious in children. The data were consistent and showed a dose response in several studies. Adjusted ORs for invasive pneumococcal disease ranged from 1.3<sup>14</sup> to 6.7<sup>15</sup> in individuals with asthma as compared to individuals without asthma, averaging around 2.0. These variations are likely due to differences in socioeconomic status, previous vaccination history and asthma severity.

This doubling in the relative risk of IPD associated with asthma needs to be balanced with the absolute risk of IPD that varies, not only per jurisdiction but also in various age groups. Therefore, a baseline incidence of 1 case of IPD per 100,000 population for a given age group will increase to 2 cases of IPD per 100,000 population in asthmatics. Moreover, all asthmatics are not equal in severity: as shown in the literature reviewed, the relative risk of IPD associated with asthma tends to be greater with increasing asthma severity. The latter needs to be taken into account at the individual level.

Currently, no data exist on the effectiveness of pneumococcal vaccines in children and adults with asthma. A small study of low quality with methodological flaws by Jung et al<sup>17</sup> suggested that pneumococcal vaccines may be less immunogenic, but also that pneumococcal colonization might induce less immune response in individuals with asthma compared to those without asthma. As such, good studies evaluating the effectiveness of pneumococcal vaccines in individuals with asthma are needed.<sup>15</sup>

## VI. RECOMMENDATIONS

Please note that provinces and territories must consider economic factors and other local programmatic/ operational factors when considering inclusion of the following recommendations in publicly funded immunization programs. Elements to take into consideration are:

- The incidence rate of IPD in various age groups (absolute risk)
- The relative risk of IPD associated with asthma, which is associated with asthma severity
- The incremental risk of IPD associated with asthma in a population with other underlying medical conditions that are already increasing their risk of IPD
- The vaccine coverage of circulating serotypes
- Herd immunity induced by vaccination programs in place.

NACI concludes that there is **good** evidence to recommend the addition of asthma – with or without prolonged use of systemic corticosteroid or associated with COPD – as a high-risk condition warranting vaccination to prevent IPD. (NACI recommendation A)

Patients who required a medical attention for asthma in the past 12 months should be vaccinated using the appropriate pneumococcal vaccine (conjugate and polysaccharide), as recommended for their age group. Asthma is not considered an immunocompromising condition in and of itself but rather a medical condition with a higher risk of IPD.

#### In Summary:

- Children 2 to 18 years of age with asthma should receive PNEU-C-13 as appropriate for their age group and an additional dose of PNEU-P-23 at least 8 weeks after the last dose of PNEU-C-13.
- Adults with asthma should receive one dose of PNEU-P-23, as other adults with chronic conditions increasing the risk of IPD, without immune suppression.
- At this time further booster doses of PNEU-C-13 or PNEU-P-23 are not recommended.

Please refer to the Canadian Immunization Guide (CIG), Chapter on Chronic Conditions for more details on vaccine type (conjugate or polysaccharide) and schedule to use. (<http://www.phac-aspc.gc.ca/publicat/cig-gci/p03-chroni-eng.php>)

## VII. SURVEILLANCE AND RESEARCH PRIORITIES

The epidemiology of invasive pneumococcal disease is changing in Canada and elsewhere, due to the use of PNEU-C-13 in the routine childhood schedule. Nationwide surveillance systems to detect these changes over time are essential. Optimal policy decisions about the use of pneumococcal vaccines requires ongoing surveillance for serotype-specific rates of invasive pneumococcal disease, serotype-specific estimates of the effectiveness of different vaccines, and continued assessment of the vaccine effectiveness and cost-effectiveness of different vaccination schedules over time.

Surveillance and research which addresses the following outstanding questions is particularly encouraged:

- What is the incidence of IPD in children and adults with asthma in Canada?
- What is the efficacy, effectiveness and immunogenicity of pneumococcal vaccines in individuals with asthma?
- What is the impact of conjugate pneumococcal vaccines use in routine infants' vaccination program on IPD in children and adults with asthma – in particular in terms of serotypes involved?
- What are the determinants of indirect protection of asthmatics (herd immunity) conferred by routine childhood pneumococcal vaccination?

## TABLES

Table 6. Summary of Evidence for NACI Recommendation(s):

STUDY DETAILS				SUMMARY	
Authors	Study Design	Study Population	Outcome Measures	Quality	Level of Evidence
FLORY ET AL <sup>12</sup>	<p>Prospective population-based surveillance study of bacteremic pneumococcal pneumonia (BPP)(n=609)</p> <ul style="list-style-type: none"> <li>30 min structured telephone interview data for those who could be contacted after their hospitalization; proxy if necessary</li> <li>Annual incidence of disease based on Poisson distribution; census data used for pop-denominator values</li> </ul>	<p>Adults in 43 of 46 acute care hospitals in the 5-county region surrounding Philadelphia, in Southeastern Pennsylvania</p> <ul style="list-style-type: none"> <li>March 31 2002-April 1 2004</li> <li><u>Case definition:</u> adults <math>\geq 18</math> with at least one blood culture drawn within 48 hours of hospital admission with growth of <i>S.pneumoniae</i>; clinical diagnosis of pneumonia provided by treating physician, residence in 1 of 5 counties and confirmation in their lab that the bacterial isolate was <i>S.pneumoniae</i></li> </ul>	<ul style="list-style-type: none"> <li>Asthma present in 25% of cases</li> <li>"For individuals with a history of asthma, the incidence was 21.1 (95% CI, 16.7, 26.6) cases per 100 000 person years compared to 8.8 (95% CI 7.9-9.8) for individuals without a history of asthma"</li> </ul> <p>"In terms of clinical risk factors, our study confirms...the association between pneumococcal disease and specific comorbidities, including asthma, diabetes, and cancer"</p>	Good	II-3
HJULER ET AL <sup>11</sup>	<p>Population-based case-control study (n=17 028 total – 1,655 cases with IPD; 15,373 controls.</p> <ul style="list-style-type: none"> <li>10 age- and gender-matched controls per case</li> </ul>	<p>Children (aged 0-17 years old) with IPD between 1977-2005 in Denmark that were singleton births</p> <ul style="list-style-type: none"> <li>IPD defined as isolation of <i>S.pneumoniae</i> from a normally sterile site</li> </ul>	<p>60 cases and 282 controls had asthma</p> <p>Adjusted IPD Rate Ratio 1.1 (95% CI 0.7, 1.6) in asthmatic children compared to control children without asthma on record</p>	Good	II-2

STUDY DETAILS				SUMMARY	
Authors	Study Design	Study Population	Outcome Measures	Quality	Level of Evidence
HSU K ET AL <sup>10</sup>	Retrospective population-based surveillance study <ul style="list-style-type: none"> <li>Standardized case report forms → Interview primary care providers - demographics and clinical info</li> </ul>	<ul style="list-style-type: none"> <li>IPD &amp; asthma status ascertained by linking 4 Danish national data sources</li> </ul> Children (<18 years) with IPD between October 2001-September 2007 from Massachusetts <ul style="list-style-type: none"> <li><u>Classified as high risk (HR) IPD</u>: sickle cell anemia, asplenia or splenic dysfunction, HIV, cochlear implants</li> <li><u>Classified as probable HR</u>: congenital immune deficiency, immunosuppressive treatment or radiotherapy, transplant, chronic heart and lung disease (including asthma if high dose oral steroids); chronic renal failure, CSF leak, diabetes, prematurity. History of hay fever or infantile eczema or cough, dyspnea, and wheezing regularly on exposure to an antigen; Pulmonary function tests showing 1 FEV1 or FVC &lt; 70%</li> </ul>	<ul style="list-style-type: none"> <li>578 of 586 cases enrolled.</li> <li>95(16%) HR/PHR; 20 (3%) asthma without corticosteroid. - mean age 5.6 years</li> <li>After adjustment for age and study year, HR/PHR more likely to be hospitalized (OR 2.75; 1.44-5.24).</li> <li>Similar clinical presentation with or without HR.</li> <li>Asthma: increased likelihood of presenting with pneumonia (65 vs. 31% if NKR p&lt;0.05).</li> </ul>	Good	II-2

STUDY DETAILS				SUMMARY	
Authors	Study Design	Study Population	Outcome Measures	Quality	Level of Evidence
		<p>predicted and another with <math>\geq 20\%</math> improvement to an FEV1 of <math>&gt; 70\%</math> predicted or methacholine challenge test showing <math>\geq 20\%</math> decrease in FEV1; Favorable clinical response to bronchodilator</p>			
JUHN Y ET AL <sup>15</sup>	<p>Population-based retrospective case control/cumulative-incidence case-control study (174 cases; 348 controls)</p> <ul style="list-style-type: none"> <li>Medical chart review</li> <li>Case to control ratio 2:1, matched by gender &amp; birthday</li> </ul> <p>66 of the cases had IPD, 108 had only pneumonia</p>	<p>Residents of Rochester Minnesota who had SPD between 1964-1983</p> <ul style="list-style-type: none"> <li>Cases of SPD defined as: sepsis, BSI, meningitis, PNC infections, pneumonia, empyema.</li> <li>Asthma status ascertained from previous study (using structured logarithm and predetermined criteria for asthma)</li> </ul>	<p>Including children and adults: OR 2.4, 95% CI (0.9-6.6)</p> <p>Including <math>&gt; 18</math> years only: Fully adjusted (smoking, ethnicity, high-risk conditions, educational status): OR 6.7, 95% CI (1.6-27.3)</p> <p>"SPD associated with a prior history of asthma in adults, suggesting that asthma increased risk for SPD"</p>	Fair (SPD, including non-bacteremic pneumococcal pneumonia outcome rather than IPD)	II-2
KLEMETS ET AL <sup>13</sup>	<p>Nationwide Finnish registry- and population-based case-control study (n= 14,067; 1282 cases, 12785 controls)</p> <ul style="list-style-type: none"> <li>10 selected age-, sex- and health-district matched controls</li> </ul>	<p>Individuals aged 18-49 years during 1995-2002</p> <ul style="list-style-type: none"> <li><u>High-risk asthma (HRA)</u>: record in the HILMO of asthma requiring <math>\geq 1</math> hospitalization in the past 12 months</li> <li><u>Low-risk asthma (LRA)</u>: entitlement to prescription</li> </ul>	<ul style="list-style-type: none"> <li>IPD associated with both LRA: mOR 2.8 (95% CI 2.1-3.6) and HRA: mOR 12.3 (95% CI 5.4-28.0)</li> </ul> <p>"Results of our national, population-based study indicate that LRA is also an independent factor moderately</p>	Good	II-2

STUDY DETAILS				SUMMARY	
Authors	Study Design	Study Population	Outcome Measures	Quality	Level of Evidence
		drug benefits and no hospitalization for asthma in the past 12 months	increasing the risk for IPD among adults 18-49 years of age"		
PILISHVILI T ET AL <sup>9</sup>	Population- and lab-based case-control study, n=3294 (cases: 782, controls: 2512) <ul style="list-style-type: none"> <li>IPD from Active Bacterial Core surveillance-CDC surveillance program</li> <li>Telephone interviews of parents or guardians using standardized questionnaire. Underlying illnesses (including asthma) collected from HC providers</li> <li>Matched median of 3 controls: case by age and zip code</li> </ul>	Children aged 3-59 months residing in certain counties in California, Colorado, Georgia, Minnesota, NY, Oregon, Tennessee and Connecticut between 2001-2004 <ul style="list-style-type: none"> <li>IPD case: isolation of <i>Pneumococcus</i> from a normally sterile site (blood, CSF, pleural fluid) or a surveillance area resident</li> </ul>	<ul style="list-style-type: none"> <li>N: 1267 IPD - 1121 eligible Multivariable log reg: (1+PCV7)</li> <li><u>Vaccinated:</u> Underlying HR condition: OR 23.9 (9.5-60.4) Daycare 1.1 (0.6-2.2)</li> <li><u>Unvaccinated:</u> Underlying HR: 4.1 (2.4-7.2) Daycare 2.0 (1.3-3.0) Black 3.5 (1.9-6.6)</li> <li><u>Risk for non-PCV7:</u> Underlying medical illness only significant in household without smoker (3.3; 2.2-5.1) Daycare both Black and White Asthma (1.5; 1.1-2.1)</li> </ul>	Good	II-2
TALBOT ET AL <sup>16</sup>	Nested matched case-control study (n=6985; 635 cases, 6350 controls) <ul style="list-style-type: none"> <li>IPD from ABC-CDC surveillance program in Tennessee</li> <li>10 aged-matched controls without IPD</li> </ul>	Individuals aged 2-49 years participating in Tennessee Medicare - state-based capitated managed health care program (TennCare) for more than one year during study period (1995-2002) <ul style="list-style-type: none"> <li>IPD "defined as isolation of <i>S.pneumoniae</i> from a</li> </ul>	<ul style="list-style-type: none"> <li>Any asthma: OR 2.4 (95% CI: 1.9-3.1)</li> <li>High-risk asthma: OR 2.6 (95% CI: 2.0-3.5)</li> <li>Low-risk asthma: OR 1.7 (95% CI: 0.99-3.0)</li> <li>No coexisting HR conditions OR 2.4 (95% CI: 1.7-3.4)</li> </ul>	Good	II-2

STUDY DETAILS				SUMMARY	
Authors	Study Design	Study Population	Outcome Measures	Quality	Level of Evidence
	<p>randomly selected from the same population as cases</p> <ul style="list-style-type: none"> <li>Adjusted for sex, race, high-risk co-existing conditions</li> </ul>	<p>normally sterile site</p> <ul style="list-style-type: none"> <li>Between 1995-2002 - 635 episodes from TennCare</li> </ul> <p><u>Ascertainment of asthma:</u></p> <p>1 of:</p> <ol style="list-style-type: none"> <li>1 or + hospital or Emergency department visit with dx code for asthma</li> <li>2 or+ Rx B-agonist</li> <li>1 or+ Rx inhaled corticosteroid, long-acting B-agonist, inhaled anti-inflammatory agents, LKT-modifying drug</li> </ol> <ul style="list-style-type: none"> <li><u>High-risk asthma:</u> 1 or+ hospitalization or ED visit AND Rx of PO steroids OR Rx of 3+ B-agonist</li> </ul> <p>CONTROLS: 10 age-matched</p>	<ul style="list-style-type: none"> <li>Coexisting HR: 2.3 (1.3-4.1) Age 2-4 (2.3; 1.4-4.0); 5-17 (4.0; 1.5-10.7); 18-49 (2.4; 1.8-3.3)</li> <li><u>Incidence:</u> Asthma: 6.1/10 000 No Asthma: 2.0/10 000</li> <li>High-risk asthma: 6.9 Low-risk asthma: 3.9</li> <li><u>In those without HR condition:</u> High-risk: 4.2 Low-risk: 2.3 No asthma: 1.2</li> </ul> <p>"Through the linkage of two large, population based databases in Tennessee, we identified an increase by more than a factor of two in the risk of invasive pneumococcal disease among persons with asthma, even after adjustment for other risk factors for the disease"</p>		
WATT ET AL <sup>14</sup>	<p>Matched case control study (118 cases and 353 controls)</p> <ul style="list-style-type: none"> <li>Age-, gender-, neighborhood-matched controls</li> </ul>	<p>Enrolled adult (≥18 years old) members of a Navajo tribe in the US with IPD between December 1999 and February 2002</p> <ul style="list-style-type: none"> <li>IPD defined as isolation of</li> </ul>	<p>Odds of having asthma were 1.3 (95% CI 0.6, 2.9) times higher in asthmatics compared to non-asthmatics in a matched, univariable analysis.</p>	Fair (Small sample size)	II-2

STUDY DETAILS				SUMMARY	
Authors	Study Design	Study Population	Outcome Measures	Quality	Level of Evidence
	<ul style="list-style-type: none"> <li>Asthma status ascertained from medical records</li> </ul>	<i>S. pneumoniae</i> from a normally sterile site <ul style="list-style-type: none"> <li>Cases identified through the Center for American Indian Health surveillance system</li> </ul>			
JUNG ET AL <sup>17</sup>	Cross-sectional Convenience sample of 16 asthmatics and 14 non-asthmatics	Asthmatics: <ul style="list-style-type: none"> <li>N=16</li> <li>Median age: 20 years</li> <li>4 previously vaccinated with PNEU-C-7</li> <li>4 previously vaccinated with PNEU-P-23</li> </ul> Non-asthmatics: <ul style="list-style-type: none"> <li>N= 14</li> <li>Median age: 28 years</li> <li>3 previously vaccinated with PNEU-C-7</li> <li>1 previously vaccinated with PNEU-P-23</li> </ul>	Serotype-specific antibodies (ELISA) – Positive if above 1.3 mg/L Median number of positive serotypes: <ul style="list-style-type: none"> <li>Asthmatics: 8.5 (IQR 5.5-15.5)</li> <li>Non-asthmatics: 15.5 (IQR 13-20).</li> </ul>	Poor	II-2
ZHAO ET AL <sup>18</sup>	Same study population as JUNG ET AL <sup>17</sup>	Same population as JUNG et AL	Serum IgG antibody levels to pneumococcal surface protein A and C (PspA, PspC), pneumococcal choline-binding protein A (PcpA), Pneumolysin (PLY) measured by ELISA  No difference between asthmatics and non-asthmatics for all antibodies measured	Poor	II-2

**Table 7. Levels of Evidence Based on Research Design**

I	Evidence from randomized controlled trial(s).
II-1	Evidence from controlled trial(s) without randomization.
II-2	Evidence from cohort or case-control analytic studies, preferably from more than one centre or research group using clinical outcome measures of vaccine efficacy.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.

**Table 8. Quality (internal validity) Rating of Evidence**

Good	A study (including meta-analyses or systematic reviews) that meets all design- specific criteria* well.
Fair	A study (including meta-analyses or systematic reviews) that does not meet (or it is not clear that it meets) at least one design-specific criterion* but has no known "fatal flaw".
Poor	A study (including meta-analyses or systematic reviews) that has at least one design-specific* "fatal flaw", or an accumulation of lesser flaws to the extent that the results of the study are not deemed able to inform recommendations.

\* General design specific criteria are outlined in Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med 2001;20:21-35.

**Table 9. NACI Recommendation for Immunization -- Grades**

A	NACI concludes that there is <b>good</b> evidence to recommend immunization.
B	NACI concludes that there is <b>fair</b> evidence to recommend immunization.
C	NACI concludes that the existing evidence is <b>conflicting</b> and does not allow making a recommendation for or against immunization; however other factors may influence decision-making.
D	NACI concludes that there is <b>fair</b> evidence to recommend against immunization.
E	NACI concludes that there is <b>good</b> evidence to recommend against immunization.
F	NACI concludes that there is <b>insufficient</b> evidence (in either quantity and/or quality) to make a recommendation, however other factors may influence decision-making.

## LIST OF ABBREVIATIONS

<b>Abbreviation</b>	<b>Term</b>
ABC	Active Bacterial Core
BPP	Bacteremic pneumococcal pneumonia
CI	Confidence ratio
COPD	Chronic obstructive pulmonary disease
FEV1	Forced expiratory volume in one second
HILMO	National Hospital Discharge Register
HIV	Human immunodeficiency virus
HRA	High-risk asthma
ICD	International Classification of Diseases (WHO)
IMPACT	Canadian Immunization Monitoring Program Active
IPD	Invasive pneumococcal disease
LRA	Low-risk asthma
NKR	No known risk
OR	Odds ratio
PNEU-C-10	Pneumococcal conjugate vaccine-10-valent
PNEU-C-13	Pneumococcal conjugate vaccine-13-valent
PNEU-P-23	Pneumococcal polysaccharide vaccine-23-valent
SPD	Serious pneumococcal disease

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## REFERENCES

1. National Advisory Committee on Immunization (NACI). Statement on the Use of Conjugate Pneumococcal Vaccine - 13 Valent in Adults (Pneu-C-13). In: (PHAC) PHAC, ed2013.
2. National Advisory Committee on Immunization (NACI). An Advisory Committee Statement (ACS). National Advisory Committee on Immunization (NACI). Statement on recommended use of pneumococcal conjugate vaccine. *Can Commun Dis Rep.* Jan 15 2002;28(ACS-2):1-32.
3. National Advisory Committee on Immunization (NACI). Update on the recommendations for the routine use of pneumococcal conjugate vaccine for infants. An Advisory Committee Statement (ACS). *Can Commun Dis Rep.* May 1 2006;32(ACS-4):1-6.
4. National Advisory Committee on Immunization (NACI). Update on the Use of Pneumococcal Vaccines in Childhood. *Can Commun Dis Rep.* 2010;36(ACS-12):1-21.
5. National Advisory Committee on Immunization (NACI). Evidence-based recommendations for immunization--methods of the National Advisory Committee on Immunization. An Advisory Committee Statement (ACS). *Can Commun Dis Rep.* Jan 2009;35(ACS-1):1-10.
6. Boikos C, Quach C. Risk of Invasive Pneumococcal Disease in Children and Adults with Asthma: A Systematic Review. *Vaccine.* 2013;31:*In Press*.
7. World Health Organization. Pneumococcal Disease. 2012; <http://www.who.int/ith/diseases/pneumococcal/en/index.html>.
8. StatsCan. Asthma, by sex, provinces and territories (Number of Persons). 2012; <http://www.statcan.gc.ca/tables-tableaux/sum-som/101/cst01/health50a-eng.htm>.
9. Pilishvili T, Zell ER, Farley MM, et al. Risk factors for invasive pneumococcal disease in children in the era of conjugate vaccine use. *Pediatrics.* Jul 2010;126(1):e9-17.
10. Hsu KK, Shea KM, Stevenson AE, Pelton SI, Members of the Massachusetts Department of Public H. Underlying conditions in children with invasive pneumococcal disease in the conjugate vaccine era. *Pediatr. Infect. Dis. J.* Mar 2011;30(3):251-253.
11. Hjuler T, Wohlfahrt J, Staum Kaltoft M, Koch A, Biggar RJ, Melbye M. Risks of invasive pneumococcal disease in children with underlying chronic diseases. *Pediatrics.* Jul 2008;122(1):e26-32.
12. Flory JH, Joffe M, Fishman NO, Edelstein PH, Metlay JP. Socioeconomic risk factors for bacteraemic pneumococcal pneumonia in adults. *Epidemiol. Infect.* May 2009;137(5):717-726.
13. Klemets P, Lyytikäinen O, Ruutu P, et al. Risk of invasive pneumococcal infections among working age adults with asthma. *Thorax.* Aug 2010;65(8):698-702.

14. Watt JP, O'Brien KL, Benin AL, et al. Risk factors for invasive pneumococcal disease among Navajo adults. *Am. J. Epidemiol.* Nov 1 2007;166(9):1080-1087.
15. Juhn YJ, Kita H, Yawn BP, et al. Increased risk of serious pneumococcal disease in patients with asthma. *J. Allergy Clin. Immunol.* Oct 2008;122(4):719-723.
16. Talbot TR, Hartert TV, Mitchel E, et al. Asthma as a risk factor for invasive pneumococcal disease. *N. Engl. J. Med.* May 19 2005;352(20):2082-2090.
17. Jung JA, Kita H, Dhillon R, et al. Influence of asthma status on serotype-specific pneumococcal antibody levels. *Postgraduate medicine.* Sep 2010;122(5):116-124.
18. Zhao H, Jung JA, Briles DE, Kita H, Tsigrelis C, Juhn YJ. Asthma and antibodies to pneumococcal virulence proteins. *Infection.* Jun 8 2013.